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AD NUMBER
AD596202
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TO:	unclassified
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LIMITATION CHANGES

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CDE TP 103

AD596202

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THE EFFECT OF WINDSPEED ON THE MIOTOGENIC POTENCY OF GB AND VX VAPOUR

by

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INV 90

Technical Paper No.103

20090213 179

June 1972

Chemical Defence Establishment, Porton Down, Salisbury, Wilts.

C.D.E. TECHNICAL PAPER NO 103

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Appendix by R.G. PICKNETT

SUMMARY

The relationship between wind speed and the potency of GB and VX vapour for the production of miosis has been studied in rabbits and humans.

Changes in windspeed have a small effect on the degree of miosis produced by GB vapour. The Ct to produce 90% miosis in humans at a wind speed of 0.01 m/s is 10 mg min/m^3 and at 2 m/s is 4 mg min/m^3; with VX vapour, however, the Ct to produce 90% miosis falls from 7 mg min/m^3 at 0.01 m/s to 0.09 mg min/m^3 at 2 m/s.

This difference between the effects of GB and VX vapour at varying wind speeds can be explained in terms of the physico-chemical properties of the two agents. A mathematical model has been developed which gives good agreement with experimental results.

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THE EFFECT OF WINDSPEED ON THE MIOTOGENIC POTENCY OF GB AND VX VAPOUR

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S. CALLAWAY and P. DIRNHUBER

INTRODUCTION

Previous work on the miotogenic potency of GB and of VX vapour (1) showed that GB vapour (dosage in mg min/m^3) was about three times as effective, when it impinged on the rabbit eye at 1.5 m/s than it was at 0.002 m/s. In further experiments it was found that VX vapour, led into goggles worn by humans, failed to produce miosis at 0.002 m/s when the concentration was approximately three times that found to be effective when directed against the rabbit eye at 1.5 m/s. Yet other experiments (1) had shown that the sensitivities of rabbit and human eyes under similar experimental conditions were not significantly different. It was therefore suspected that air velocity had a much greater influence on the miotogenic potency of VX vapour than on that of GB vapour. The present paper describes experiments designed to test this hypothesis, and proposes a mathematical model which gives good agreement with the experimental findings.

MATERIALS

Freshly prepared GB of 97% purity and VX of 86% purity as checked by chemical analysis (2) were used to prepare the vapour generators.

METHODS

Flow rate of vapour-carrying air

In all experiments the volume-flow rate of air carrying the GB or VX vapour to the eye was monitored by means of a rotameter. The same set of flow values, viz. 0.1, 0.5, 1.0, 2.0 and 5 l/min was used consistently, a particular flow rate being selected for a given experiment. The size of the jet delivering the air current to the eye and its orientation relative to the corneal surface was always the same for a given volume-flow rate. Because of this consistency each volume-flow corresponded to a certain windspeed near the corneal surface. It seems likely that the speed of the air and agent vapour current in proximity to this surface is the major factor determining the magnitude of the physiological effect of a given dosage of agent. Attempts were therefore made to measure the

speed of the air current near the eye.

Measurements were carried out by means of a thermistor anemometer. The probe was the thermistor, type U 23 US (STANTEL), which consists of a spherical semiconductor bead of 0.5 mm diameter suspended from extremely thin wires. The anemometer was calibrated by placing the probe in the axis of tubes of known diameter. Readings were taken at pre-set volume-flow rates of air through the tubes. The corresponding air speeds were calculated and plotted against the anemometer readings.

Because of its small size the probe could be expected to cause only little interference with a given pattern of air flow near a surface. It was not possible however to use this anemometer during actual animal or human exposures because intermittent contact of the bead with the corneal surface would have been difficult to avoid without intolerable restraint of the human or animal involved. The probe was therefore mounted on plaster casts of human or rabbit heads and the thermistor bead was carefully placed at 0.5 to 1 mm distance from the surface of the eyeball. The exposure conditions of the live experiments were closely imitated and anemometer readings corresponding to pre-set volume-flow readings on the rotameter were noted.

Agent vapour generators

GB

The GB vapour generator was similar to that used in earlier experiments on humans (1). Dry nitrogen at a rate of 0.1 1/min was passed through the generator and the effluent was mixed with air to produce the required flow rate.

Dilution of GB in diethyl phthalate was such that severe miosis could be achieved after three successive exposure periods totalling approximately one hour.

VX

Rubber contaminated with VX served as the vapour source in two types of generator, straight tube and spiral tube (Fig. 1).

A straight tube generator (Fig. 1a) was used for flow rates up to 2 1/min. It consisted essentially of a 16 cm length of bicycle valve tubing (outside diameter 5.3 mm, wall thickness 2 mm). VX was evenly applied to the outer surface over a length of 150 mm, leaving 5 mm at each end clean. The surface density of the VX was in the range of 8 to 24 g/m^2 according to the vapour concentration required.

The total amount of VX per tube was 6 to 18 mg. After storage for 24 hours the contaminated rubber tubing was threaded into a polythene tube and the ends fastened by inserting short pieces of tightly fitting glass tubes.

Nitrogen was passed through the generator at one of three pre-set flow rates viz. 0.5, 1.0 and 2.0 1/min. Bubbler samples for chemical estimation of the VX vapour concentration (2) were taken at the same flow rate that was being used for experimental exposures on a given day.

The spiral tube generator (Fig. 1b) was used at the highest flow rate only, i.e. 5 1/min. Red rubber tubing of 5.5 mm external diameter, wall thickness, 2.3 mm, length 4.4 m was wound round a disc of 50 mm diameter to form a flat spiral supported by thin wire spokes. The outer surface of the tubing (area 0.077 m^2) was evenly contaminated with VX to a surface densiry of 8 g/m^2. After storage for 24 hours the spiral was sealed into a double-walled Mylar-Polythene bag and the ends of the tubing brought out through the seal.

The concentration of agent vapour emerging from the generators was sampled and measured as previously described (1).

Subjects

The subjects of these experiments were 47 albino rabbits and 63 healthy volunteer servicemen. Details of the numbers exposed to VX and GB under specified conditions are listed in Table 1.

Application of the agent vapour to the eyes

For the flow rates between 0.1 and 2.0 1/min goggles were used on humans (1) and rabbits (Fig. 2) both for GB add VX vapour. In the human exposures the jet admitting the vapour to the goggle space was near the temporal corner of the eye. In rabbit exposures the jet was placed approximately in the middle of the goggle space, parallel to the eye shield of the goggle. It was found that with jets in these positions the airspeed near the corneal surface was not critically dependent on the exact orientation of the jet.

In GB exposures the same generator was used for both eyes. In experiments with the lowest flow rate (0.1 1/min per eye) both eyes were exposed simultaneously; at all higher windspeeds the left and right eye were treated in succession.

In VX exposures a separate generator, monitored by its own flowmeter, was used for the left and right eye. At half time generators were interchanged to ensure equal dosage to both eyes. The VX vapour

passed into the goggle space directly from the outlet of the straight-tube generator.

For the flow rate of 5 l/min (corresponding to an air-speed of 2.2 m/s near the cornea) the eyes of humans and rabbits were exposed to the free jet emerging from a tube of 5.5 mm internal diameter, from a distance of 20-30 mm.

The method of successive exposure as described earlier (1) was used in all experiments.

Measurement of miosis was carried out as described in (1) which also contains definitions of the terms used.

RESULTS

Estimation of dosage causing 90% loss of pupil area (ECt 90) for a given agent and air velocity

Fig. 3 serves as an example to show the type of data obtained from a series of experiments with a given air-speed; in this case VX was applied to human eyes with an air-speed of 0.01 m/s. Each point in the graph represents one miosis measurement on a given eye after a certain cumulative dosage Ct. The degree of miosis (percent pupil area decrease) is plotted against Ct (mg min/m^3) on log-probability co-ordinates. The straight line, representing the regression of probit pupil area decrease, on log-dosage, was fitted by probit analysis (3) and an estimate of the ECt 90 and its fiducial limits were obtained. The ECt 90 was selected in preference to the more accurately determined ECt 50 since it was considered that a decrease of only 50% in the light reaching the retina of the eye does not constitute a significant handicap to vision (4).

Experiments were done on humans with VX vapour at three different windspeeds and on rabbits at five different windspeeds. With GB vapour the effects of three windspeeds were studied on humans and on rabbits. Table 1 lists the values for ECt 90 and their 95% fiducial limits calculated from this series of experiments. Column 2 of Table 1 gives the actual vapour concentrations of GB and VX used.

Relationship between ECt 90 and air velocity

In Fig. 4 the ECt 90 shown in Table 1 is plotted against air-velocity on logarithmic coordinates. The two lines of shallow slope refer to GB and the two lines of steeper slope to VX. The upper line of each pair represents the human results. It can be seen that for GB the Ct necessary to produce a 90% decrease in pupil area is not

greatly dependent on air velocity. For instance in humans a 90% miosis results from exposure to a Ct of 10 mg min/m^3 at an air velocity of 0.01 m/s or to a Ct of 4 mg min/m^3 at 2 m/s. In the case of VX, on the other hand, the effect of air velocity is considerably greater. At a velocity of 0.01 m/s 90% miosis is caused by a Ct of 7 mg min/m^3 whereas at an air velocity of 2 m/s a Ct of only 0.09 mg min/m^3 has the same effect.

DISCUSSION

The present work shows that GB and VX vapour in still air have approximately the same miotogenic potency whereas at a moderate windspeed (2 m/s) VX vapour is approximately 50 times more effective than GB. The increase in windspeed from practically still air to a velocity of 2 m/s causes only a 3 to 4 fold increase in the miotogenic potency of GB vapour whereas in the case of VX vapour the factor could be as much as two orders. This very different effect of windspeed on VX and GB vapour with regard to the miotogenic potency may be satisfactorily explained in terms of the physico-chemical properties of these agents. VX has almost no vapour pressure in aqueous solution in the tear fluid moistening the eyeball because it is rapidly transformed into an ionic species which is involatile though still physiologically active. GB on the other hand has an appreciable vapour pressure over its aqueous solution. The finite vapour pressure of GB in the boundary layer of still air next to the surface film of liquid on the cornea provides, in effect, a back pressure tending to allow the agent to evaporate from the eye surface, whereas ionisation of VX in solution reduces this back pressure to negligible proportions and ensures a net inward transfer rate much more sensitive to windspeed.

A practical consequence of the present findings is that an inefficient respirator or loosely-fitting goggles could, by cutting down the circulation of VX-laden air around the eye, provide a useful degree of protection against the development of miosis.

This conclusion must be balanced against the consideration that a concentration of VX vapour below the limit of the field detection kit, viz. 0.02 to 0.04 mg/m^3 (5), could provide a severe degree of miosis at moderate wind speeds.

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TABLE 1

ESTIMATES OF ECt 90 OF GB AND VX AT DIFFERENT AIR VELOCITIES

Air velocity m/s	Vapour concentration mg/m^3			ECt 90 and 95% fiducial limits (mg min/m^3)		Number of measurements	
				MAN VX			Persons
0.01	0.72;	0.92		5.65	(4.76 − 7.33)	32	8
0.07	0.04;	0.10;	0.42	1.96	(1.52 − 2.87)	34	7
2.2	0.025;	0.11		0.0727	(0.0597−0.0950)	35	10
				GB			
0.002	0.005;	0.010; 0.014		13.85	(6.00 − 32.02)	62	26
0.07	0.68;	0.74;	1.09	7.29	(5.36 − 14.70)	28	7
2.2	1.1;	2.8;	5.5	3.83	(2.54 − 9.53)	21	5
				RABBITS VX			Rabbits
0.002	0.137			2.27	(1.72 − 3.51)	15	3
0.02	0.038; 0.052; 0.162			1.47	(1.05 − 2.47)	8	2
0.06	0.10			0.61	(0.43 − 1.05)	9	2
0.20	0.065			0.130	(0.123−0.141)	6	2
2.2	0.02			0.057	(0.038−0.146)	14	6
				GB			
0.002	0.019; 0.15;	0.78		7.68	(4.92 − 19.5)	43	1
0.06	0.54			3.11	(2.53 − 5.25)	8	2
1.50	0.015; 0.82			2.71	(0.91 − 9.03)	46	19

APPENDIX

by R.G. PICKNETT

VX in aqueous solution reacts very rapidly with hydrogen ions to give a protonated species of effectively zero vapour pressure. On the other hand, GB in aqueous solution has an appreciable vapour pressure, and at pH 7.8 - 8.0 will remain unchanged for a time long compared with the exposure times used in this investigation. Using a simple physical model, it can be shown that these facts can account for the influence of air velocity on the effectiveness of GB and VX in causing miosis.

The model used is illustrated in Fig. 5. It is assumed that air blown across or against the eye forms a stagnant layer next to the surface, while, further out, the air is well-mixed and constantly replaced. (This is a simplification of reality, but is good enough to provide a qualitative answer to the problem). Thus the concentration of organic vapour in the air outside the stagnant layer will be constant and equal to the incoming concentration C_∞; that in the stagnant layer will be controlled by molecular diffusion.

Next, it is assumed that the aqueous layer on the eye is so thin that the nerve agent concentration C_w in it is uniform. For low concentrations Raoult's law predicts that

$$C_o = kC_w, \qquad \ldots 1$$

where C_o is the nerve agent concentration in the air just above the water, and k is an equilibrium constant.

Finally, it is assumed that the eye can absorb sufficient nerve agent to keep the concentration constant at its surface. This simplifies the expression for the mass rate of diffusion R' from the water into the eye to:

$$R' = KC_w, \qquad \ldots 2$$

where K is another constant.

If h is the thickness of the stagnant layer of air, the mass rate of diffusion R'' from the air to the water is

$$R'' = (C_\infty - C_o)D/h, \qquad \ldots 3$$

D being the molecular diffusion constant of the vapour.

On exposure of the eye to vapour, C_w rapidly increases to an equilibrium value where:

$$R' = R'' \qquad \ldots 4$$

Eliminating C_O and C_W between equations 1 to 4, the following is obtained:

$$R' = \frac{C_\infty DK}{Kh + Dk}$$

The ECt for miosis is inversely proportional to R', and hence

$$(ECt) = B\left\{\frac{h}{C_\infty D} + \frac{k}{C_\infty K}\right\} ,$$

B being the constant of proportionality. For GB, this equation applies in *toto*, the subscript G being used:

$$(ECt)_G = \frac{B}{C_\infty}\left\{\frac{h}{D_G} + \frac{k_G}{K_G}\right\} \qquad \dots 5$$

For VX, k is effectively zero since C_O is zero due to the ionization in solution, and thus, using the subscript V:

$$(ECt)_V = \frac{Bh}{C_\infty D_V} \qquad \dots 6$$

Equations 5 and 6 contain the solution of the problem. It is clear that the ECt values for GB and for VX can be very different, and that they depend on h, the thickness of the stagnant air layer. Further, it is well known that the thickness of this layer changes with air velocity, being thinner the higher the velocity. For VX, therefore, it follows from equation 6 that the ECt decreases with increasing air velocity. For GB, on the other hand, the ECt need not decrease at all with increasing air velocity, provided the second term on the right hand side of equation 5 is much greater than the first.

To demonstrate the prediction of the theory, the results for VX were used to estimate values of $Bh/C_\infty D_V$ from equation 6 for different air velocities. The assumption was then made that B, C_∞, D and h were the same for VX and GB, and graphs of ECt versus air velocity were drawn for a range of values of $Bk_G/C_\infty K_G$. The predicted curves for GB are shown in figure 6, and demonstrate that the theory provides an adequate qualitative description of the experimental results. The one exception is the ECt for the lowest air velocity with man, which is much less than theory predicts. However, this discrepancy is not thought to be significant since it probably arises from the linear plot taken to represent the experimental VX results. A more correct representation would be a curve tending to constant ECt 90 at low velocity, and this would remove the anomaly.

It should be borne in mind that the approximations used make the theory only qualitative. For example, the physical model employed of a stagnant boundary layer is not strictly correct. Also it has been assumed that VX is completely protonated in solution, whereas it is known

that pK for the protonation is 8.9 (6).   Thus, at pH 7.8 - 8.0,
the range of values found for tear fluid (7), about 10% of the VX
in solution remains unionized.   The theory could be modified to
take these matters into account, but the additional complication
would not be justifiable while there are no values available for
many of the parameters used.

(a) **STRAIGHT TUBE**
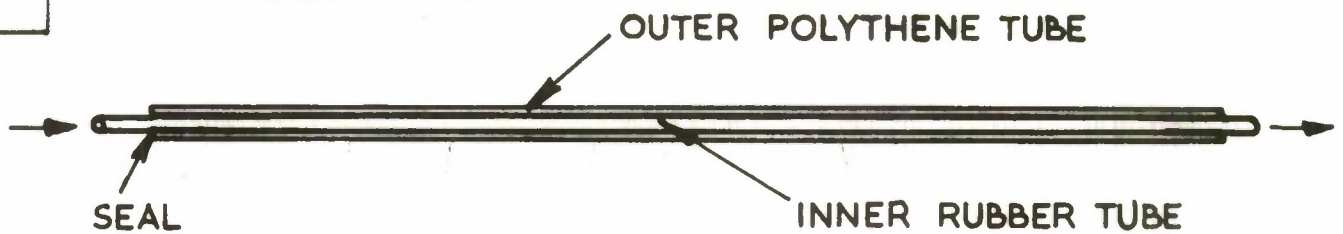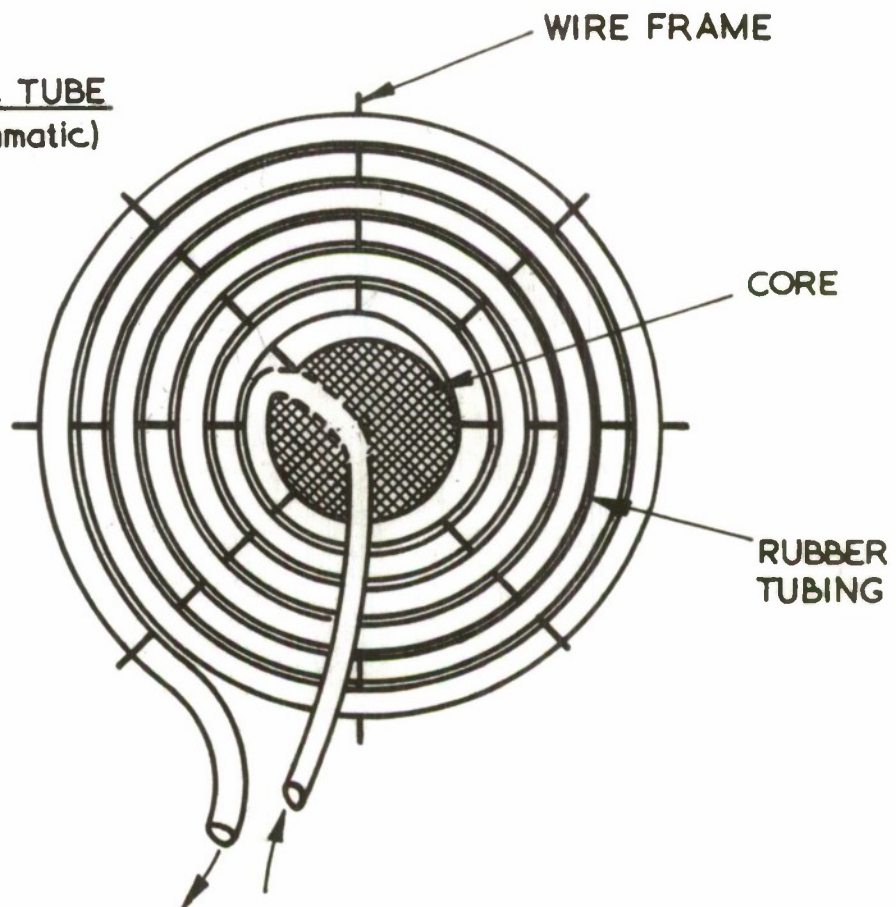
OUTER POLYTHENE TUBE

SEAL

INNER RUBBER TUBE

WIRE FRAME

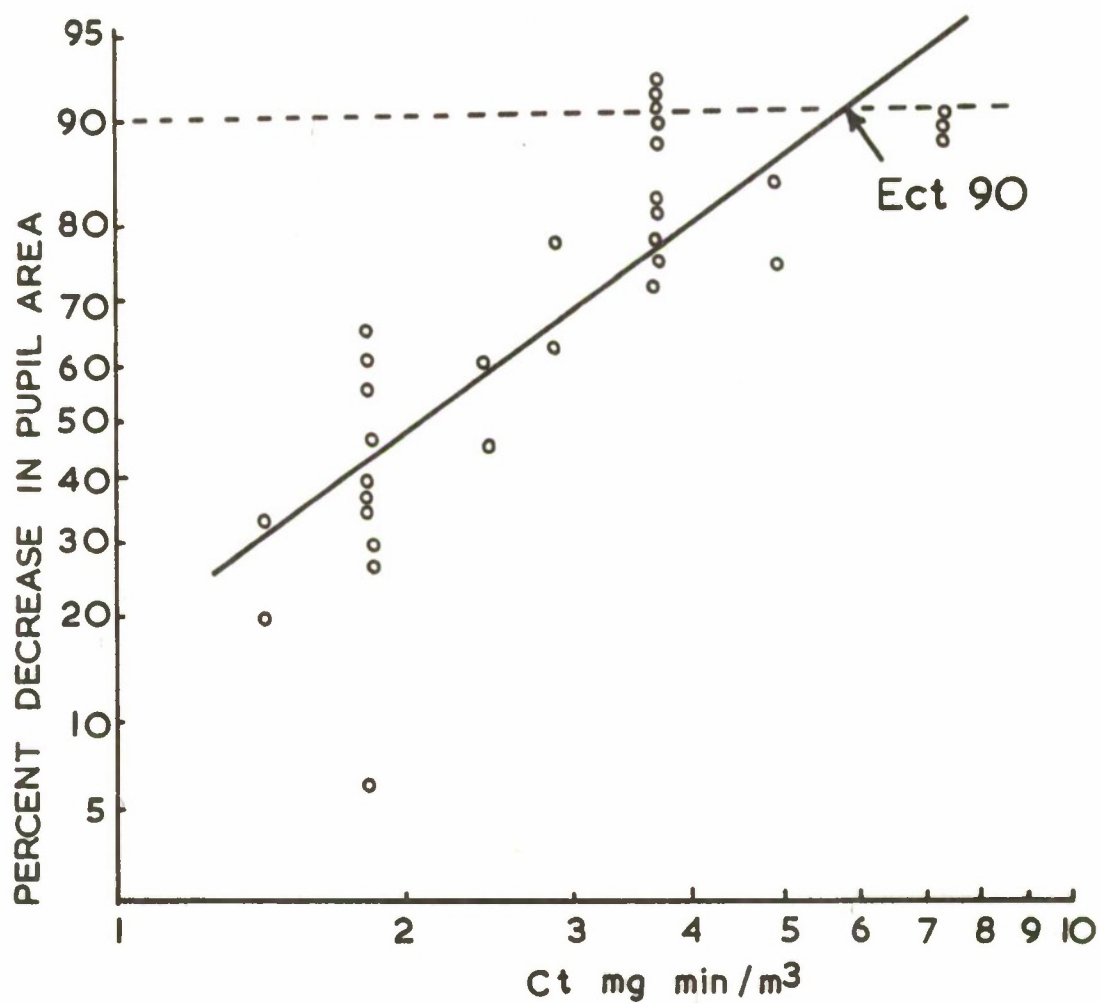(b) **SPIRAL TUBE**
(diagrammatic)

CORE

RUBBER
TUBING

VX VAPOUR GENERATORS

FIG. 1.

Fig. 2.   APPLICATION OF VAPOUR TO THE RABBIT EYE

TYPICAL EXPERIMENT ON HUMAN SUBJECT TO SHOW
METHOD OF ESTIMATING Ect 90 FOR MIOSIS

FIG .3

G.B₁ MAN

G.B₁ RABBIT

VX₁ MAN

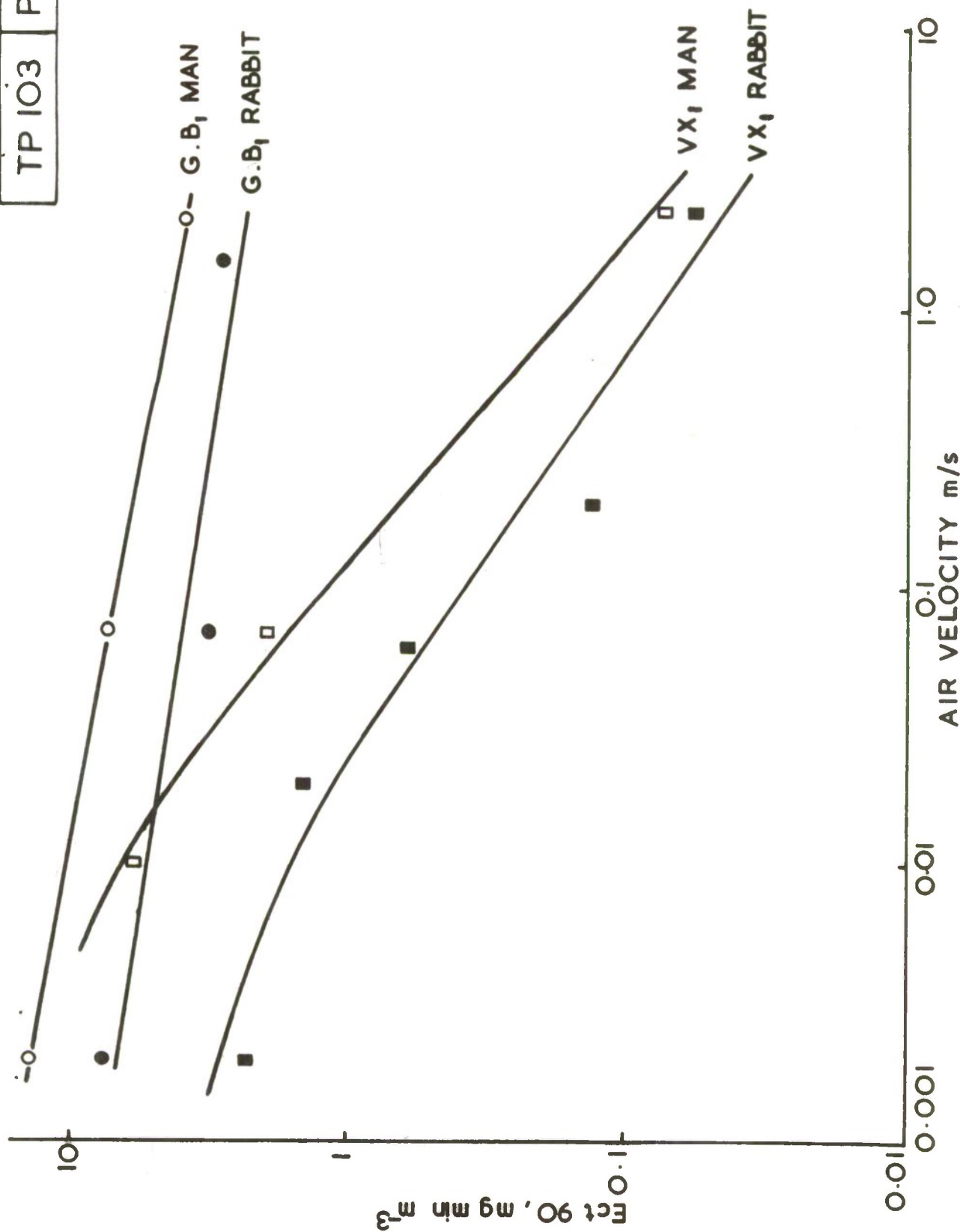VX₁ RABBIT

Ect 90 , mg min m⁻³

AIR VELOCITY m/s

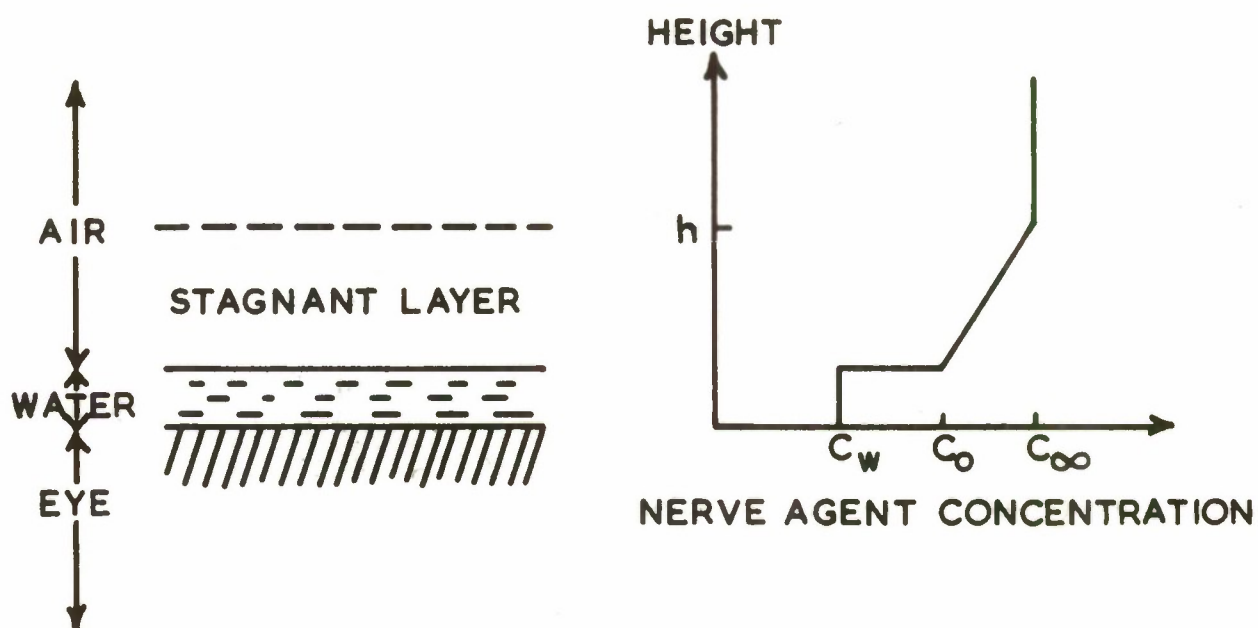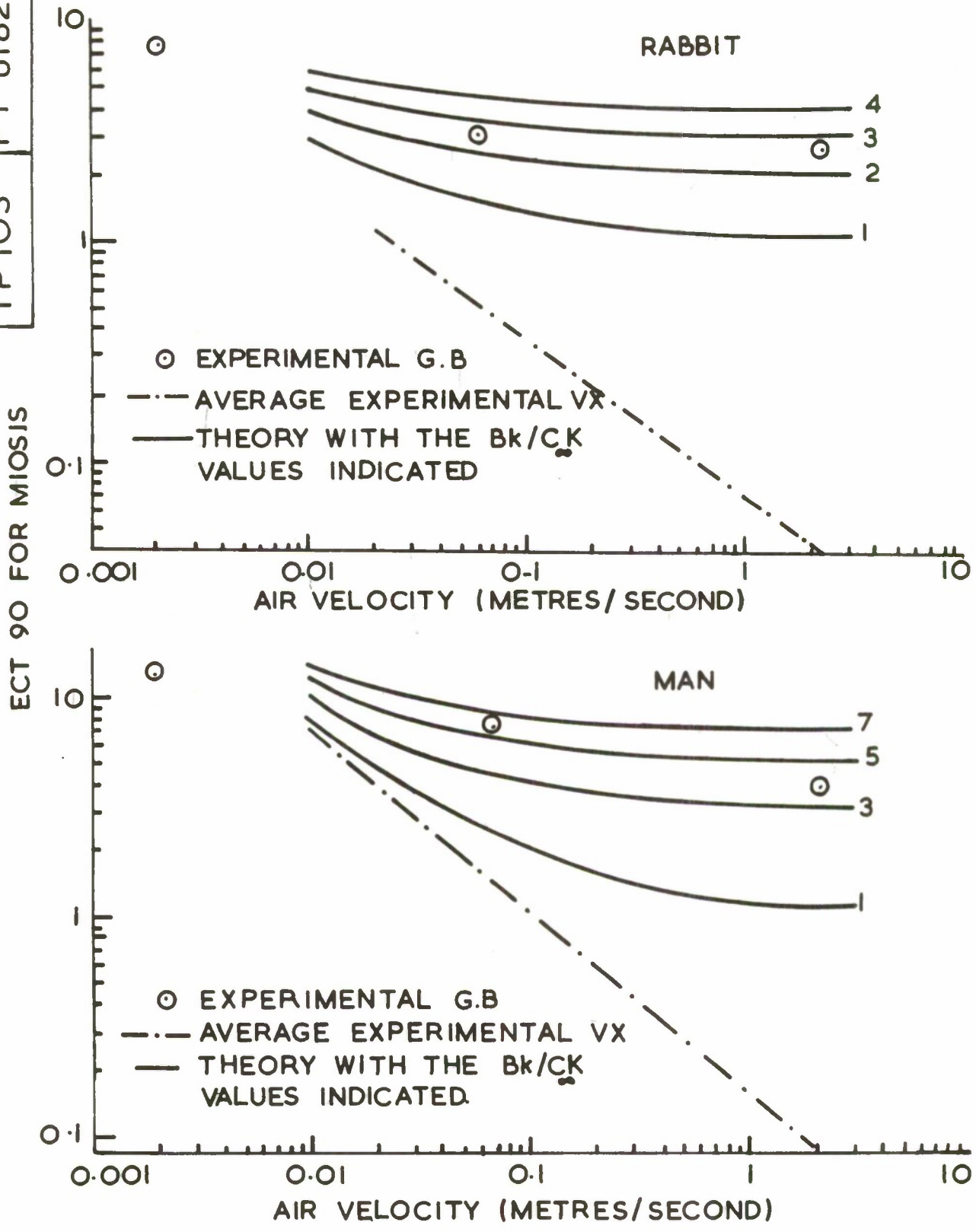RELATIONSHIP BETWEEN AIR VELOCITY AND Ect 90 FOR MIOSIS

FIG . 4

ILLUSTRATION OF PHYSICAL MODEL USED
TO PREDICT DEPENDENCE OF ECT 90 ON AIR VELOCITY

FIG.5

THEORETICAL GB CURVES COMPARED WITH EXPERIMENT

FIG. 6

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Date of Search: 12 December 2006

Record Summary:
Title: The effect of windspeed on the miotogenic potency of GB and VX vapours
Covering dates 1972 Jun 01 - 1972 Jun 30
Availability Open Document, Open Description, Open on Transfer
Former reference (Department) CDE TP 103
Held by The National Archives, Kew

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